
Liver-Directed Human Amniotic Epithelial Cell Transplantation Improves Systemic Disease Phenotype in Hurler Syndrome Mouse Model.

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Public Summary:

Hurler syndrome, also known as mucopolysaccharidosis type I (MPS-I), is a rare inborn error of metabolism that results in the accumulation of glycoprotein due to a deficiency of lysosomal function. Available therapies are limited in their ability to address skeletal and neurological disease phenotypes, which are crucial for the patients' quality of life. This study in a mouse model of the disease shows that transplanted human amniotic epithelial cells (hAECs) can compensate for the missing enzyme activity long term and improve disease phenotypes, including facial bone morphology, joint mobility, and sensorimotor coordination. As hAECs are readily available nontumorigenic cells, the presenting cell therapy approach is a novel alternative for treating MPS-I Hurlers syndrome.

Scientific Abstract:

Mucopolysaccharidosis type 1 (MPS1) is an inherited lysosomal storage disorder caused by a deficiency in the glycosaminoglycan (GAG)-degrading enzyme alpha-L-iduronidase (IDUA). In affected patients, the systemic accumulation of GAGs results in skeletal dysplasia, neurological degeneration, multiple organ dysfunction, and early death. Current therapies, including enzyme replacement and bone marrow transplant, improve life expectancy but the benefits to skeletal and neurological phenotypes are limited. In this study, we tested the therapeutic efficacy of liver-directed transplantation of a placental stem cell, which possesses multilineage differentiation potential, low immunogenicity, and high lysosomal enzyme activity. Unfractionated human amniotic epithelial cells (hAECs) were transplanted directly into the liver of immunodeficient Idua knockout mouse neonates. The hAECs engraftment was immunohistochemically confirmed with anti-human mitochondria staining. Enzyme activity assays indicated that hAECs transplantation restored IDUA function in the liver and significantly decreased urinary GAG excretion. Histochemical and micro-computed tomography analyses revealed reduced GAG deposition in the phalanges joints and composition/morphology improvement of cranial and facial bones. Neurological assessment in the hAEC treated mice showed significant improvement of sensorimotor coordination in the hAEC treated mice compared to untreated mice. Results confirm that partial liver cell replacement with placental stem cells can provide long-term (>20 weeks) and systemic restoration of enzyme function, and lead to significant phenotypic improvement in the MPS1 mouse model. This preclinical data indicate that liver-directed placental stem cell transplantation may improve skeletal and neurological phenotypes of MPS1 patients. Stem Cells Translational Medicine 2017.

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